

FIGURE 1

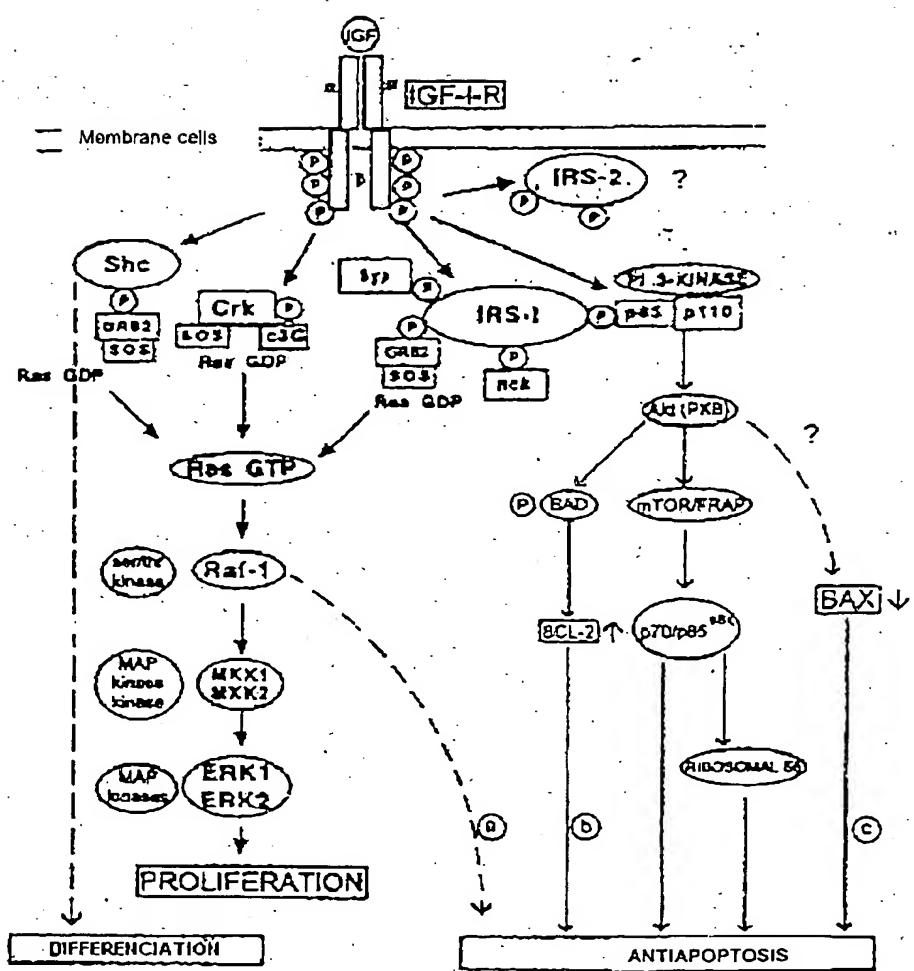


FIGURE 2

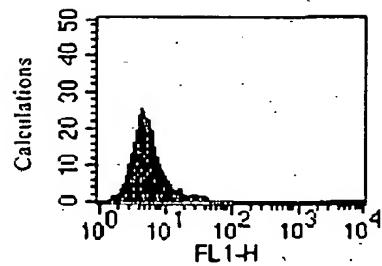


FIGURE 3A

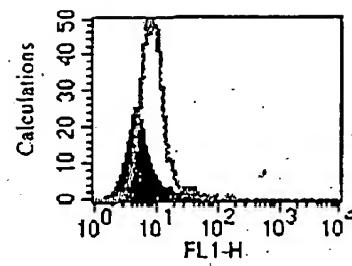


FIGURE 3B

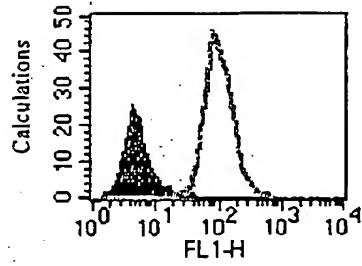
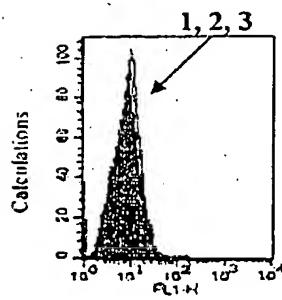
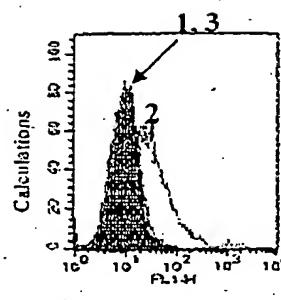


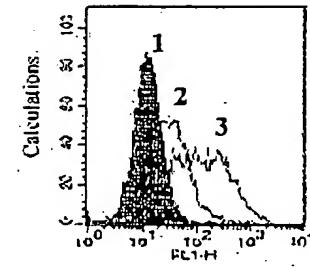
FIGURE 3C



Nontransfected cells



IGF-IR+ cells



IR+ cells

FIGURE 4A

FIGURE 4B

FIGURE 4C

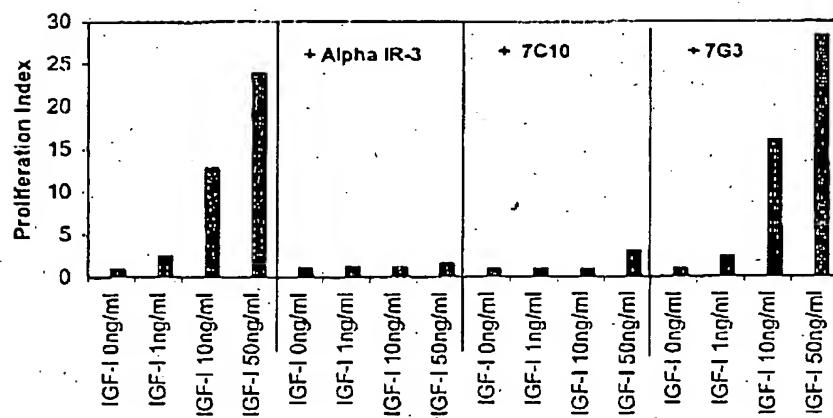


FIGURE 5

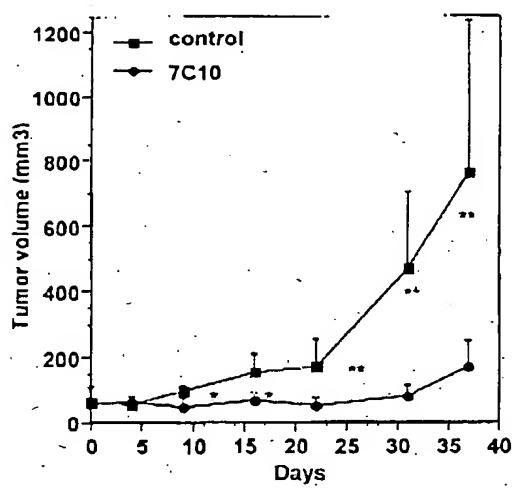


FIGURE 6A

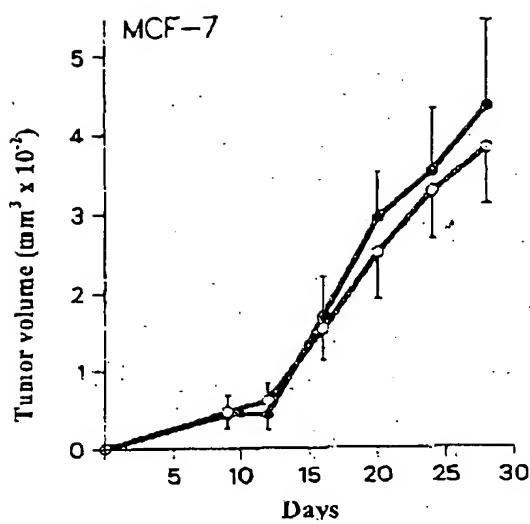


FIGURE 6B

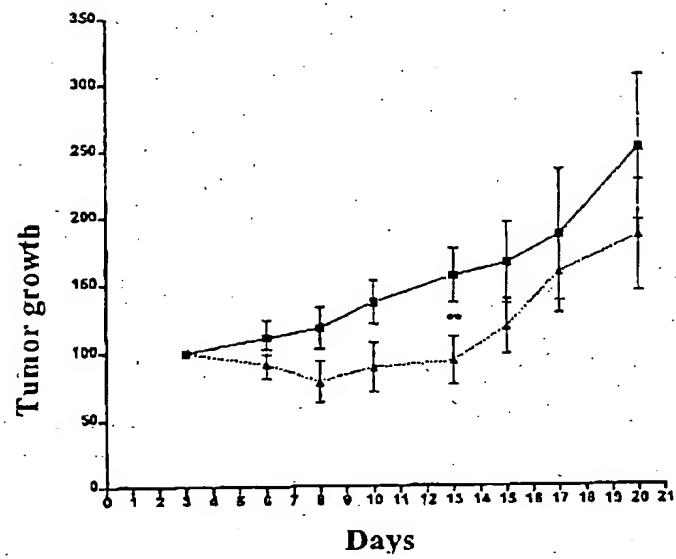


FIGURE 6C

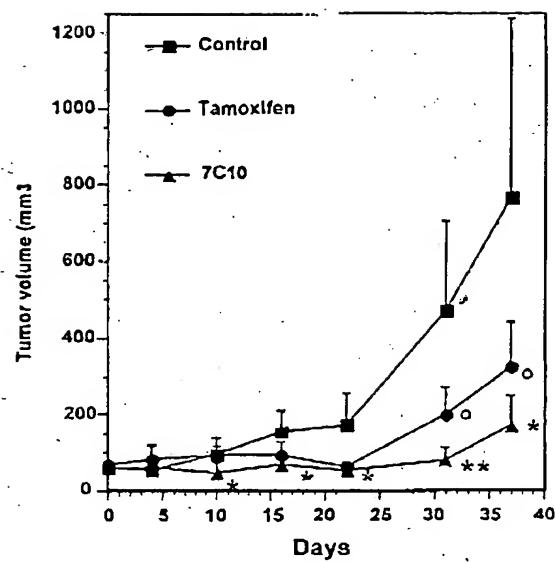


FIGURE 7

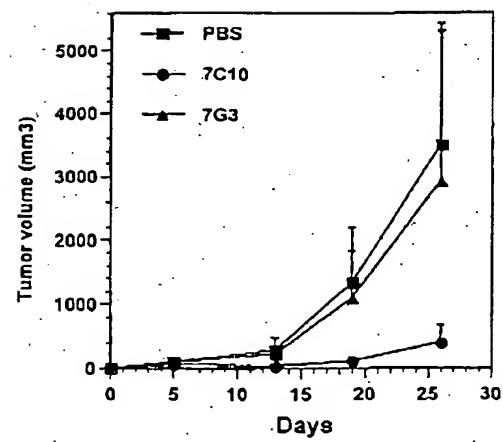


FIGURE 8A

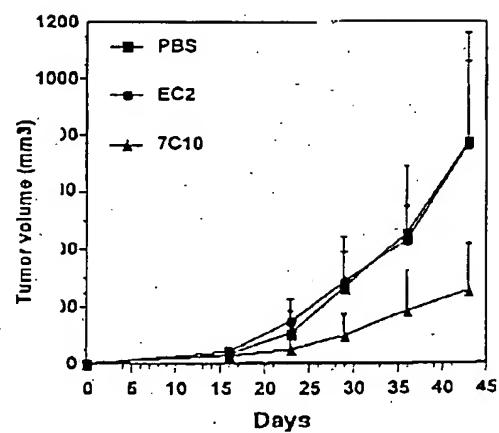


FIGURE 8B

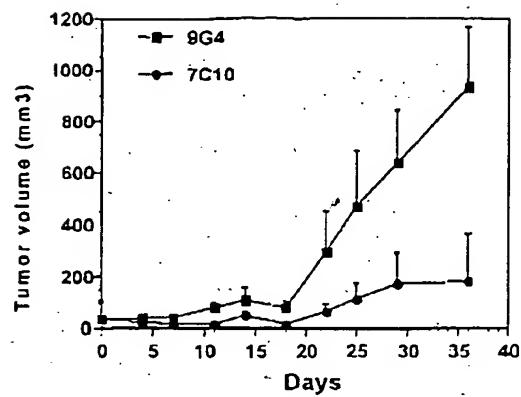


FIGURE 8C

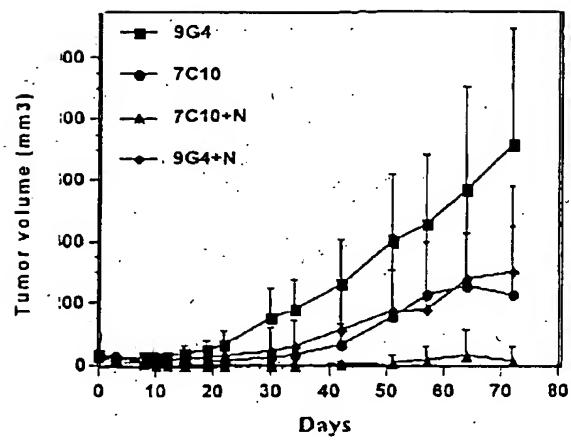


FIGURE 9

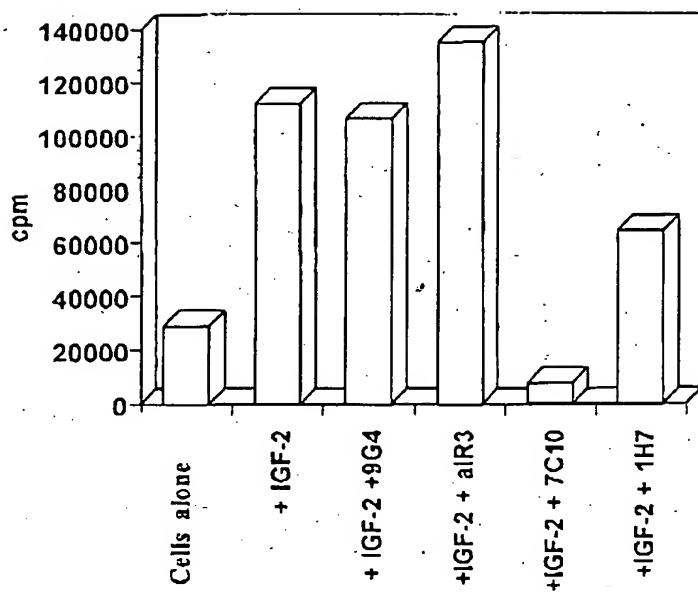


FIGURE 10

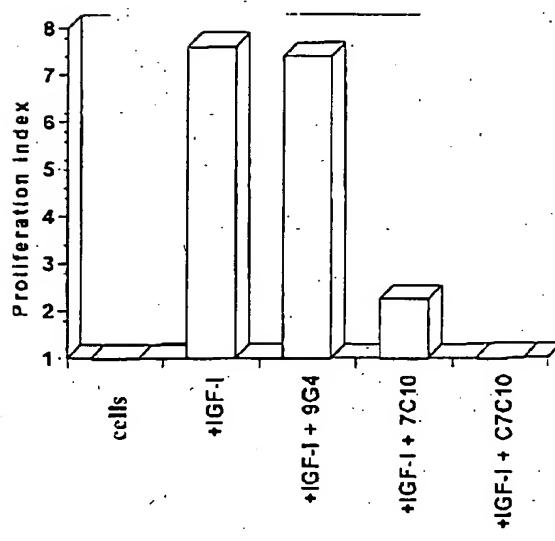


FIGURE 11

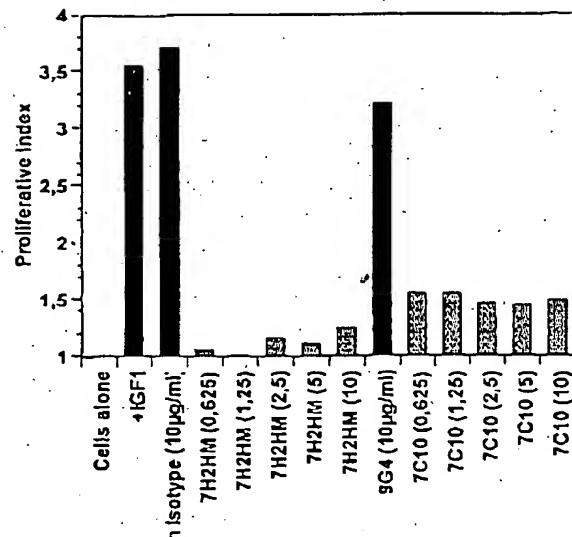


FIGURE 12

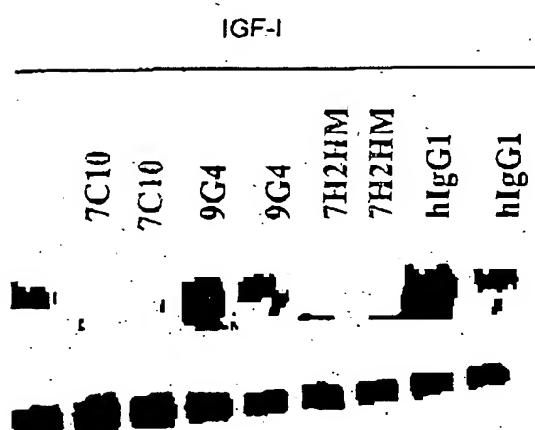


FIGURE 13

ATGAAGTTGCCTGTTACCTGTTGGTGTGATGTTCTGGATTCCTGCTTCGAGAAGTGAT 60
 1 TACTTCAACGGACAATCCGACAACCACCACTACAGACCTAAGGACGAAGTCTCACTA
 ATGAAGTTGCCTGTTAGGCTGTTGGTGTGCT
 oligo MKV-1 L M F W I P A S R S D -
 3' end leader peptide
 GTTTGATGACCCAAATTCCACTCTCCCTGCCTGTCAGTCTGGAGATCAAGCCTCCATC 120
 61 CAAAACACTGGGTTAAGGTGAGAGGGACGGACAGTCAGAACCTCTAGTCGGAGGTAG
 V L M T Q I P I S L P V S L G D O A S T -
 TCTTCCAGATCTAGTCAGAGCATTTGACATAGTAATGAAACACCTATTACATGGTAC 180
 121 AGAACGTCTAGATCACTCTCGTAACATGTATCATTACCTTGTTGGATAATGTTACCATG
 S C R S S O S I V H S N G N T Y L Q W Y -
 CDR 1
 CTCCAGAAACCCAGGTCACTCTCCAAACCTCTGATCTACAAAGTTCCAACCGACTTAT 240
 181 GACGTCTTGGTCCAGTCAGAGGTTTCGAGGACTACATCTTCAGGGTTGGCTGAAATA
 L Q K P G Q S P K L L I Y K V S N R L Y -
 CDR 2
 GGGGTCCCAGACAGGTTCACTGGCAGTGGATCAGGGACAGATTCACACTCAAGATCAGC 300
 241 CCCCAGGGTCTGTCCAAGTCACCGTCACCTAGTCCCTGTCTAAACTGTGAGTTCTAGTCG
 G V P D R F S G S G S G T D F T L K I S -
 AGCGTGGAGGCTGAGGATCTGGAGTTATTACTGCTTCAGCTCACATGTTCCGTGC 360
 301 TCGCACCTCCACTCTAGACCCCTCAAATAATGACGAAGTCCAAGTGTACAAGGCACC
 S V E A E D L G V Y Y C F Q G S H V P W -
 CDR 3
 GG
 ACGTTCGGTGGAGGCACCAAGCTGAAATCAAACGGGCTGATGCTGCACCAACTGTATCC 420
 361 TGCAAGCCACCTCCGTGGTCTGACCTTAGTTGCCGGACTACGACGTGGTTGACATAGG
 T F G G G T K L E I K
 MKC oligo
 TAGAAGGGTGGTAGGTCA
 ATCTTCCCACCATCCAGT
 421 438
 TAGAAGGGTGGTAGGTCA

FIGURE 14

ATGATGGTCTTAAGTCTTCTGTACCTCTGACAGCCATTCTGGTATCCTGTCTGATGTA 60
 1 -----+-----+-----+-----+-----+-----+
 TACTACCACAATTCAAGAACATGGACAACTGTCGGTAAGGACCATAGGACAGACTACAT
 MHV-12 ATGATGGTCTTAAGTCTTCTGTACCT
 MHV-8 ATGAGAGTGCTGATTCTTTGTG
 L L T A I P G I L S D V -
 3' end leader peptide
 CAGCTTCAGGAGTCAGGACCTGGCCTCGTGAAACCTTCTCAGTCTGTCTCACCTGC 120
 61 -----+-----+-----+-----+-----+-----+
 GTCGAAGTCCTCAGTCTGGACCGGAGCACTTGGAAAGAGTCAGAGACAGAGAGTGGACG
 Q L Q E S G P G L V K P S O S L S L T C -
 TCTGTCACCCGCTACTCCATCACCGGTGGTTATTATGGAACTGGATCCGGCAGTTCCA 180
 121 -----+-----+-----+-----+-----+-----+
 AGACAGTGGCCGATCACCTAGTGGCCACCAATAACCTTGACCTAGGCCGTCAAAGGT
 S V T G Y S I T G G Y L W N W I R Q F P -
 CDR 1
 CGAAACAAACTGGAGTGCATGGGCTACATAAGCTACGACGGTACCAATAACTACAAACCA 240
 181 -----+-----+-----+-----+-----+-----+
 CCTTTGTTGACCTCACCTACCCGATGTATTCCATGCTGCCATGGTTATTGATGTTGGT
 G N K L E W M G Y I S Y D G T N N Y K P -
 CDR 2
 TCTCTCAAAGATCGAACATCCATCACTCGTGACACATCTAAGAACAGTTTCTGAAG 300
 241 -----+-----+-----+-----+-----+-----+
 AGACAGTTCTAGCTAGAGGTACTGAGCACTGTGTAGATTCTGGTCAAAAGGACTTC
 S L K D R I S I T R D T S K N Q F F L K -
 TTCAATTCTGTGACTAATGAAGACACAGCTACATATTACTGTGCAAGATACTGGTAGGGTC 360
 301 -----+-----+-----+-----+-----+-----+
 AACTTAAGACACTGATTACTCTGTGTCGATCTATAATGACACGTTCTATCCCATCCAG
 L N S V T N E D T A T Y Y C A R Y G R V -
 CDR 3
 GGG
 TTCTTTGACTACTGGGCCAAGGCACCACTCTCACAGTCTCCTCAGCCAAACGACACCC 420
 361 -----+-----+-----+-----+-----+-----+
 AAGAAAATGATGACCCCGTTCCGTGGTAGAGGTGTCAGAGGAGTCGGTTTGCTGGG
 F F D Y W G Q G T T L T V S S
 oligo MHC-1
 GGTAGACAGATAGGTGAC
 CCATCTGTCTATCCACTG
 421 -----+----- 438
 GGTAGACAGATAGGTGAC

FIGURE 15

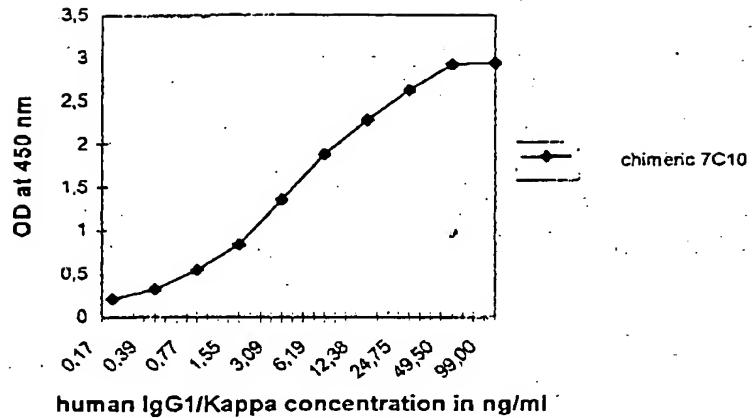


FIGURE 16

3 7 CDR 1
 7C10 VL mouse DVLMTQIPLSLPVSLGDQASISC RSSQSIVHSNGNTYLQ
 DRB1-4.3 T E
 C94-5B11'CL T E
 Kabat sgII mouse .. V .. T .. L .. E

CDR 2
 7C10 VL mouse WYLQKPGQSPKLLIY KVSNRLY GVPDRFSGSGSGTDFTL
 DRB1-4.3 FS
 C94-5B11'CL FS
 Kabat sgII mouse FS ..

77 CDR 3
 7C10 VL mouse KISSVEAEDLGVYYC FQGSHVPWT FGGGKLEIK
 DRB1-4.3 ... R F .. S .. D ..
 C94-5B11'CL ... R
 Kabat sgII mouse ... R .. T .. Y ..

FIGURE 17

CDR 1

7C10 VL mouse DVLMTQIPLSLPVSLGDQASISC RSSQSIVHSNGNTYLO
 GM607 .IV...S.....TP.EP.....LL....YN..D
 DPK15/A19 .IV...S.....TP.EP.....LL....YN..D
 Kabat sgII hu .IV...S.....TP.EP.....LL..D.XX..X

CDR 2

7C10 VL mouse WYLQKPGQSPKLLIY KVSNRLY GVPDRFSGSGSGTDFTLK
 GM607Q.... LG...AS
 DPK15/A19Q.... LG...AS
 Kabat sgII huQ.... L...AS

CDR 3

7C10 VL mouse ISSVEAEDLGVYYC FQGSHVPWT FGGGTKLEIK
 GM607 ..R.....V..... M.ALQT.Q...Q...V...
 DPK15/A19 ..R.....V..... M.ALQT.
 Kabat sgII hu ..R.....V..... M.ALQX.R...Q...V...

FIGURE 18

CDR 1

7C10 VL mouse DVLMTQIPLSLPVSLGDQASISC RSSQSIVHSNGNTYLO
 GM 607 .IV...S.....TP.EP.....LL....YN..D
 7C10 VL Humanized 1 ..V...S.....TP.EP.....
 7C10 VL Humanized 2 .IV...S.....TP.EP.....

CDR 2

7C10 VL mouse WYLQKPGQSPKLLIY KVSNRLY GVPDRFSGSGSGTDFTL
 GM 607Q.... LG...AS

7C10 VL Humanized 1Q....

7C10 VL Humanized 2Q....

CDR 3

7C10 VL mouse KISSVEAEDLGVYYC FQGSHVPWT FGGGTKLEIK
 GM 607 ...R.....V..... M.ALQT.Q...Q...V...
 7C10 VL Humanized 1 ...R.....V..... Q...V...
 7C10 VL Humanized 2 ...R.....V..... Q...V...

FIGURE 19

MluI

1 GTCACAAACGCCTGCCGCCACCATGAAGTCCCTGTTAGGCTGTTGGTGCTGATGTTCTGG
1 CAGCTTGGCAGCCGGTGGTACTTCAACGGACAATCCGACAACCACGACTACAAGACC 60

M K L P V R L L V L M F W -

Peptide leader

61 TTTCTGCTTCCAGCAGTGTGATGATGACTCAGTCTCCACTCTCCCTGCCCGTCACC
61 AAAGGACGAAGGTGTCAGTACAACACTACTGAGTCAAGAGGTGAGAGGGACGGGAGTGG 120

2 F P A S S S D V V M T O S P L S L P V T -

121 CCTGGAGAGCCGGCTCCATCTCTGCAGGTCTAGTCAGAGCATTGTACATAGTAATGGA
121 GGACCTCTCGGCCGGAGGTAGAGGACGTCCACATCAGTCTGTAACATGTATCATTACCT 180

CDR 1

P G E P A S I S C R S S Q S I V H S N G -

KpnI

181 AACACCTATTGCAATGGTACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCTGATCTAT
181 TTGGATAAACGTTACCATGGACGTCTCCGTCCGTAGAGGTGTCGACCTACATA 240

N T Y L Q W Y L Q K P G Q S P O L L I Y -

241 AAAGTTCTAATCGGCTTATGGGTCCCTGACAGGTTCAGTGGCAGTGCATCAGGCACA
241 TTTCAAAGATTAGCCGAAATACCCCAGGGACTGTCCAAGTCACCGTCACCTAGTCCGT 300

CDR 2

K V S N R L Y G V P D R F S G S G S G T -

301 GATTTTACACTGAAAATCAGCAGAGTGGAGGCTGAGGATGTTGGGTTTATTACTGCTTT
301 CTAAAATCTGACTTTAGTCGTCACCTCCACTCCTACAACCCCAAATAATGACGAAA 360

D F T L K I S R V E A E D V G V Y Y C F -

361 CAAGGTTACATGTTCCGTGGACGTTGGCCAAAGGGACCAAGGTGAAAATCAAACGTGAG
361 GTTCCAAGTGTACAAGGCACCTCCAAGCCGGTCCCTGGTCCACCTTAGTTGCACTC 420

CDR 3

O G S H V P W T F G Q G T K V E I K

BamHI

421 TGGATCCTCTGCG 433

ACCTAGGAGACGC

FIGURE 20

MluI

1 CTCAGAACGCCTGCCACCATGAAGTTGCCTGTTAGGCTGTTGGTGTATGTTCTGG
 1 CAGTCCTTGCCTGCCACGGCGGTGGTACTTCACACGACAATCCGACAACCAGACTACAGACC 60

M K L P V R L L V L M F W -
 Leader peptide

61 TTTCCCTGCTTCCAGCAGTGATATTGTGATGACTCAGTCCTCCACTCTCCCTGCCGTACCC
 61 AAAGGACGAAGGTCTGTCACTACACACTACTGAGTCAGAGGTGAGAGGGACGGGAGTGG 120

F P A S S S D I V M T Q S P L S L P V T -

121 CCTGGAGAGGCCGGCTCCATCTCTGCAGGTCTAGTCAGAGCATTGTACATAGTAATGGA
 121 GGACCTCTCCCCCGAGGTAGAGGACGTCCAGATCAGTCGTAAACATGTATCATTACCT 180

CDR 1
P G E P A S I S C R S S Q S I V H S N G -

181 KpnI
 AACACCTATTTGCAATGGTACCTGCAGAACGCCAGGGCAGTCCTCACAGCTCCTGATCTAT
 181 TTGTGGATAAACGTTACCATGGACGTCTCCGTCCCGTCAGAGGTGTCGAGGACTAGATA 240

N T Y L C W Y L Q K P G Q S P Q L L I Y -

241 AAAGTTCTAATCGGCTTATGGGGTCCCCTGACAGGTTCACTGGCAGTGGATCAGGCACA
 241 TTTCAGAGATAGCCGAAATACCCCAAGGGACTGTCCAAGTCACCGTCACCTAGTCCGTGT 300

CDR 2
K V S N R L Y G V P D R F S G S G S G T -

301 GATTTTACACTGAAAATCAGCAGAGTGGAGGCTGAGGATGTTCCGGTTATTACTGCTTT
 301 CTAAAATGTGACTTTAGTCGTCTCACCTCCACTCCTACACCCCCAAATAATGACGAAA 360

D F T L K I S R V E A E D V G V Y Y C E -

361 CAAGGTTCACATGTTCCGTGGACGTTGGCCTAACGGACCAAGGTGGAAATCAAACCTGAC
 361 GTTCCAAGTGTACAAGGCACCTGCAAGGCCGGTCCCTGGTTCCACCTTAGTTGCACTC 420

CDR 3
Q G S H V P W T F G Q G T K V E I K

BamHI
 421 TGGATCCTCTGCG 433
 ACCTAGGAGACGC

FIGURE 21

17 27 CDR 1
7C10 VH DVQLQESGPGLVKPSQSLSLTCSVTGYSIT GGYLWN WIRQ
AN03' CL S..Y.....
Kabat sgI(A) E.....S.....T.....D... S..WN. ...

CDR 2
7C10 VH FPGNKLEWMG YISYDGTNNYKPSLKD RISITRDTSKNQFFL
AN03' CL N...N...N...N ..
Kabat sgI(A) S.STY.N...S Y..

84 CDR 3
7C10 VH KLNSVTNEDTATYYCAR YGRV-FFDY WGQGTTLT^VS
AN03' CL T..... E.YGY.....
Kabat sgI(A) Q.....T..... G.YGYG.....V....

FIGURE 22

Rch 1 30 CDR 1 Rch 2
7C10 VH mouse DVQLQESGPGLVKPSQSLSLTCSVTGYSIT GGYLWN WIRQ
human Kabat sgII Q.....T.....T.S.G.VS SYWS.. ...
human VH FUR1' CL Q.....ET.....T.S....S S..Y.S ..
human Germeline Q.....ET.....T.S....S S..Y.S ..

Rch 2 48 CDR 2 67 71 Rch 3
7C10 VH mouse FPGNKLEWMG YISYDGTNNYKPSLKD RISITRDTSKNQFFL
human Kabat sgII P..KG...I. R.Y.S.STX.N....S .VT.SV.....S.
human VH FUR1' CL P..KG...I. SMFHS.SSY.N....S .VT.SV.....S.
human Germ-line P..KG...I. S.YHS.STY.N....S .VT.SV.....S.

Rch 3 CDR 3 Rch 4
7C10 VH mouse KLNSVTNEDTATYYCAR YGRVFFDY WGQGTTLT^VS
human Kabat sgII ..S...AA...V..... ELPGGYDVLV....
human VH FUR1' CL Q.R...AA...V..... GRYCSSTSCNWFDPLV....
human Germeline ..S...AA...V.....

FIGURE 23

	30 CDR 1	48
7C10 VH mouse	DVQLQESGPGLVKPSQSLSLTCVTGYSIT	<u>GGYLWN</u> WIRQFPGNKLEWMG
human germline	Q.....	ET.....T.S.... <u>S</u> S..Y.GP..KG... <u>I</u> .
VH Humanized 1	Q.....	ET.....T.S.....P..KG.....
VH Humanized 2	Q.....	ET.....T.S.....P..KG...I.
VH Humanized 3	Q.....	ET.....T.S.... <u>S</u>P..KG...I.
CDR 2		67 71
7C10 VH mouse	<u>YISYDGTNNYKPSLKD</u>	RISITRDTSKNQFFLKLNSVTNEDTATYYCAR
human germline	S.FHS.SSY.N....S	<u>VT.SV</u>S...S...AA...V.....
VH Humanized 1T.S.....S...S...AA...V.....
VH Humanized 2	<u>VT.S</u>S...S...AA...V.....
VH Humanized 3	<u>VT.SV</u>S...S...AA...V.....
CDR 3		
7C10 VH mouse	<u>YGRVFFDY</u>	WGQGTTLTVSS
human germlineLV....
VH Humanized 1LV....
VH Humanized 2LV....
VH Humanized 3LV....

FIGURE 24

MluI

1 GTCAGAACGCGTGCCGCCACCATGAAAGTGTGAGTCTGTTGTACCTCTTGACACCCATT 60
1. CAGTCTTGCACGGCGGTGGTACTTCACAACCTCAGACAACTGGAGAACTGTCGGTAA

M K V L S L L Y L L T A I -
Leader peptide
CCTGGTATCCTGTCTCAGGTGCAGCTTCAGGAGTCG/GGCCAGGACTGGTGAAGCCTCG 61
61 G G A C C A T A G G A C A G A G T C C A C G T C G A A G T C U C T C A G C C C G G G T C C T G A C C A C T T C G G A A G C 120

P G I L S Q V Q L Q E S T P G L V K P S -
GAGACCCCTGTCCTCACCTGCACTGTCTCTGGTTACTCCATCACCCGTCCTTATTTATGG 121 121 C T C T G G G A C A G G G A G T G G A C G T G A C A G A G A C C A A T G A G G T A G T G G C C A C C A A T A A A T A C C 180
30 CDR 1
E T L S L T C T V S G Y S T T G G Y L W -
A A C T G G A T A C G G C A G C C C C A G G G A A G G G A C T G G A G T C G A T G G G T A T A T C A G C T A C G A C 181 181 T T G A C C T A T G C C G T C G G G G T C C C C T G A C C T C A C C T A C C C C A T A T A C T C G A T G C T G 240
48
N W I R Q P P G K G L E W M G Y I S Y D -
KpnI
GGTACCAATAACTACAAACCCCTCCCTCAAGGATCCAATCACCATATCACGTGACACGTCC 241 241 C C A T G G T T A T T G A T G T T G G G A G G C A G T C C T A G C T T A G T G G T A T A G T G C A C T G T G C A G G 300
CDR 2 67 71
G T N N Y K P S L K D R I T I S R D T S -
A A G A A C C A G T T C T C C C T G A A G C T G A G C T C T G T G A C C G T G C G G A C A C T G C A G T G T A T T A C 301 301 T T C T T G G T C A A G A G G G A C T T C G A C T C G A G A C A C T G G C G A C G C C T G T G A C G T C A C A T A A T G 360
K N Q F S L K L S S V T A A D T A V Y Y -
T G T G C G A G A T A C G G T A G G G T C T T C T T G A C T A C T G G G G C A G G G A A C C C T G G T C A C C G T C 361 361 A C A C G C T C T A T G C C A T C C C A G A A G A A A C T G A T G A C C C C G G T C C C T T G G G A C C A G T G G C A G 420
CDR 3
C A R Y G R V F F D Y W G Q G T L V T V -
BamHI
TCCTCAGGTGAGTGCATCCTCTGCG 421 421 445
1. AGGAGTCCACTCACCTAGGAGACGC
S S -

FIGURE 25

MluI

1 GTCAGAACGCGTGCCGCCACCATGAAAGTGTGAGTCTGTTGTACCTCTTGACAGCCATT
 60 CAGTCTTGGCCACGGCGGTGGTACTTTCACAACTCAGACAAACATGGAGAACTGTCGGTAA

M K V L S L L Y L L T A I
 Leader peptide

61 CCTGGTATCCTGTCTCAGGTGCAGCTTCAGGAGTCGGGCCAGGACTGGTGAAGCCTTCG
 120 GGACCATACCAACAGAGTCCACGTCGAAGTCCTCAGCCCGGGTCTGACCAACTTCGGAAGC

P G I L S Q V Q L Q E S G P G L V K P S -

121 GAGACCCCTGTCCTCACCTGCACTGTCTCTGTTACTCCATCACCGGTGCTTATTATCG
 180 CTCTGGACAGGGAGTGGACGTGACAGAGACCAATGAGCTAGTCGCCACCAATAATACC
 30 CDR 1
 E T L S L T C T V S G Y S I T G G Y L W -

AACTCCATAACGGCAGCCCCAGGCAAGGGACTGGAGTGGATCCCCTATATCAGCTACGAC
 181 240 TTGACCTATGCCGTGGGGGTCCCCCTGACCTCACCTAGCCCATATAGTCGATGCTG
 48
 N W I R Q P P G K G L E W I G Y I S Y D -

KpnI

241 GGTACCAATAACTACAAACCCCTCCCTCAAGGATCGAGTCACCATATCACGTGACACGTCC
 300 CCATGGTTATTGATGTTGGAGGGAGTCCCTAGCTCAGTCGTATAGTCGACTGTGCAGG
 CDR 2
 67 71
 G T N N Y K P S L K D R V T I S R D T S -

AAGAACCAAGTCTCCCTGAAGCTGAGCTCTGTGACCCCTCGGGACACTGCAGTGTATTAC
 301 360 TTCTTGGTCAAGAGGGACTTCGACTCGAGACACTGGCGACGCCGTGACGTACATAATG
 K N Q F S I K I S S V T A A D T A V Y Y -

TGTGGAGATAACGGTAGGGCTTCTTGACTACTGGGCCAGGGAACCCCTGCTACCGTC
 361 420 ACACCCCTCATGCCATCCCAGAAGAAACTGATGACCCCCGGTCCCTGGGACCAAGGGCAG
 CDR 3
 C A R Y G R V F E D Y W G Q G T L V T V -

BamIII

421 445
 TCCTCAGGAGTGGAGTGGATCCTCTGCG
 AGGAGTCCACTCACCTAGGAGACGCC
 S S -

FIGURE 26

MluI

1 CTCAGAACGCCTGCCACCATGAAAGTGTGAGTCTGTTGACCTCTTGACAGCCATT
 1 CAGTCTTGCGCACGGCGGTGGTACTTTCACAACTCACACACATGGAGAACTGTCGGTAA

M K V L S L L Y L L T A I -
 Lcader peptide

61 CCTGGTATCCTGTCTCAGGTGCAGCTTCAGGAGTCGGGCCAGGACTGGTGAAGCCTTCG
 61 GGACCATAGGACAGAGTCCACGTCGAAGTCCCTCAGCCGGTCCCTGACCACTTCGGAAGC

P G I L S Q V Q L O E S G F G L V K P S -
 121 GAGACCCCTGTCCCTCACCTGCACGTCTGTTACTCCATCAGCGGTGGTTATTTATGG
 121 CTCTGGGACAGGGAGTGGACGTGACAGAGACCAATGAGGTAGTCGCACCCAATAAATACC
 30 CDR 1
 E T L S E T C T V S G Y S I S G G Y I W -
 181 AACTGGATACGGCAGCCCCCAGGGAAACCCACTGGAGTGGATCGGGTATATCAGCTACGAC
 181 TTGACCTATGCCGTGGGGTCCCTCCCTGACCTCACCTACCCATATACTCGATGCTG
 48
 N W I R Q P P G K G L E W I G Y I S Y D -
 KpnI
 241 GGTACCAATAACTACAAACCCCTCCCTCAAGGATCGAGTCACCATATCAGGGACACGTCC
 241 CCATGGTTATTGATGTTGGGAGGGACTTCCTAGCTCAGGGTATAGTCACCTGTGCAGG
 67 71
 C T N N Y K P S L K D R Y T I S V D T S -
 301 AAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCCCTGGGACACTGCAGTGTATTAC
 301 TTCTGGTCAAGAGGGACTTCGACTCGAGACACTGGCGACGCCGTGACGTACATAATG
 560
 K N Q F S L K L S S V T A A D T A V Y Y -
 361 TGTGCGAGATACTGGTAGGGCTTCTTCACTACTGGGGCCAGGGACCCCTGGTCACCGTC
 361 ACACGCTCTATGCCATCCAGAAGAAACTGATGACCCGGTCCCTGGGACCACTGGCAG
 CDR 3
 C A R Y G R V F F D Y W G Q G T L V T V -
 BamHI
 421 TCCTCAGGTGAGTGGATCCTCTGGC
 421 445
 AGGAGTCCACTCACCTAGGAGACGC
 S S

FIGURE 27

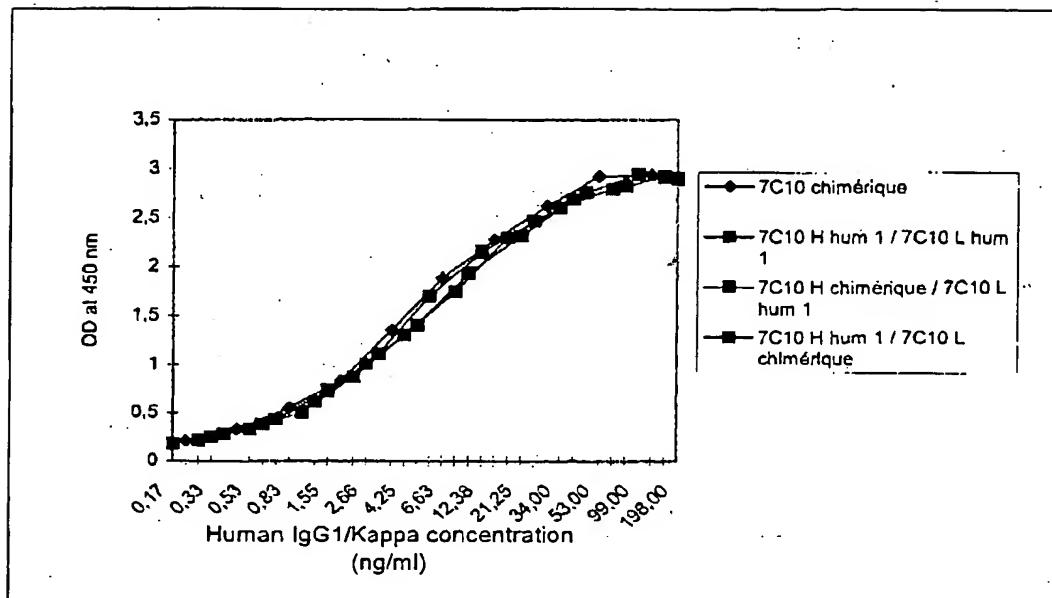


FIGURE 28

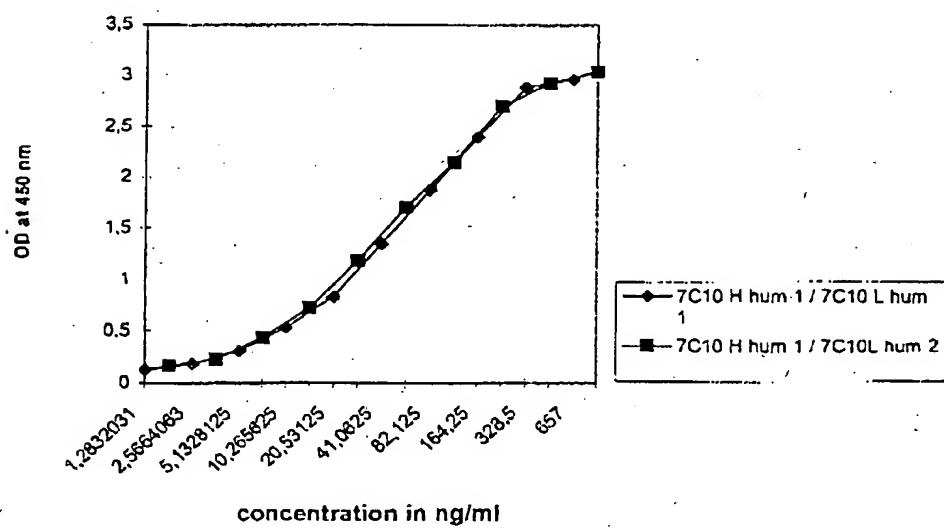


FIGURE 29

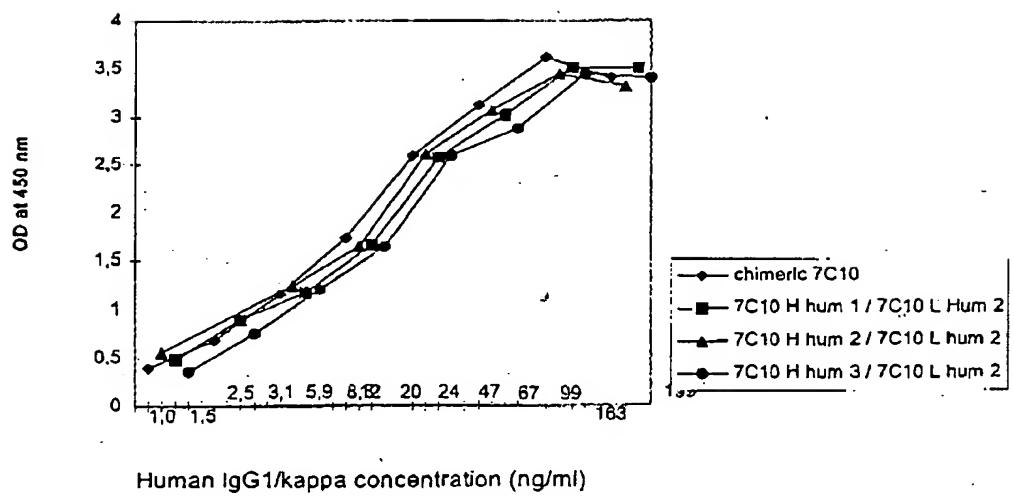
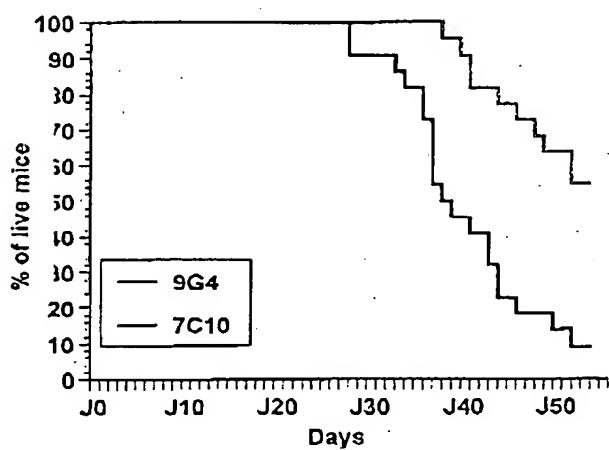


FIGURE 30



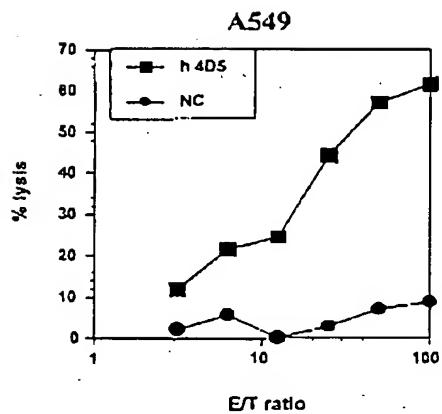


FIGURE 32A

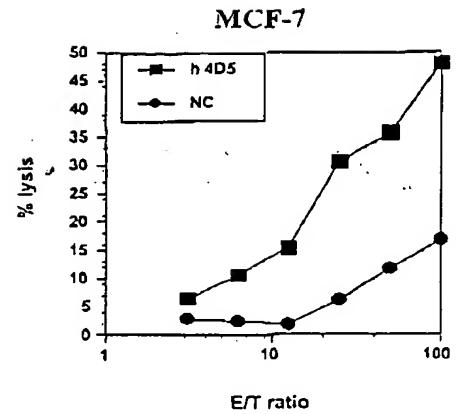


FIGURE 32B

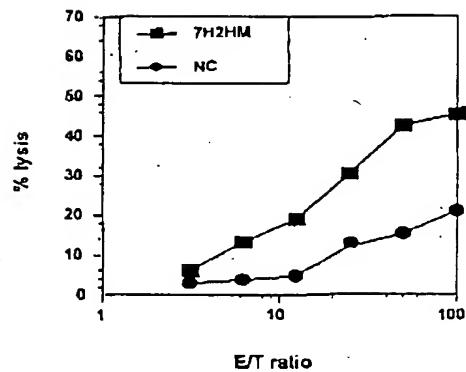


FIGURE 32C

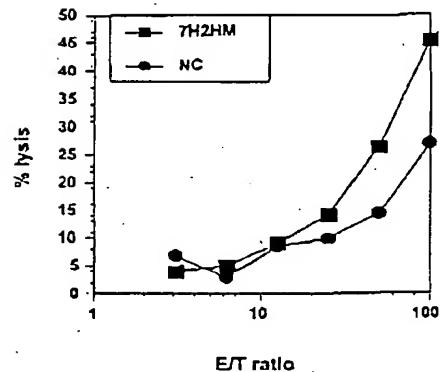
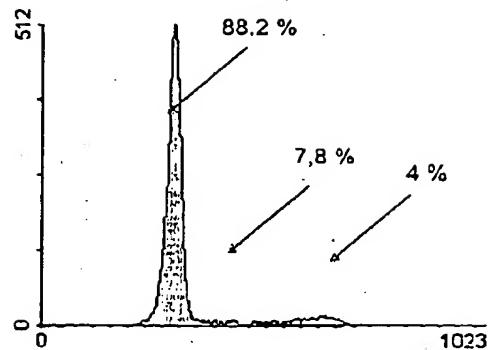


FIGURE 32D

- IGF1



+ IGF1 (50 ng/ml)

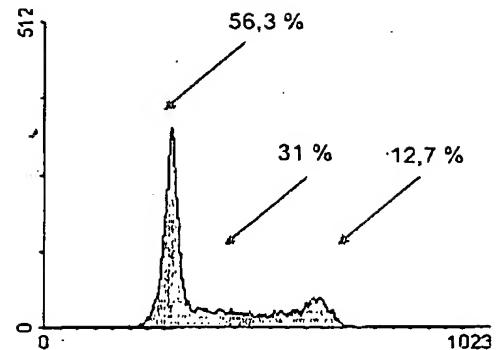


FIGURE 33A

FIGURE 33B

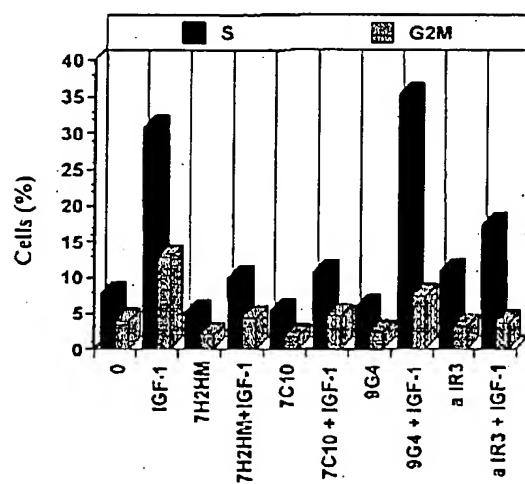


FIGURE 33C

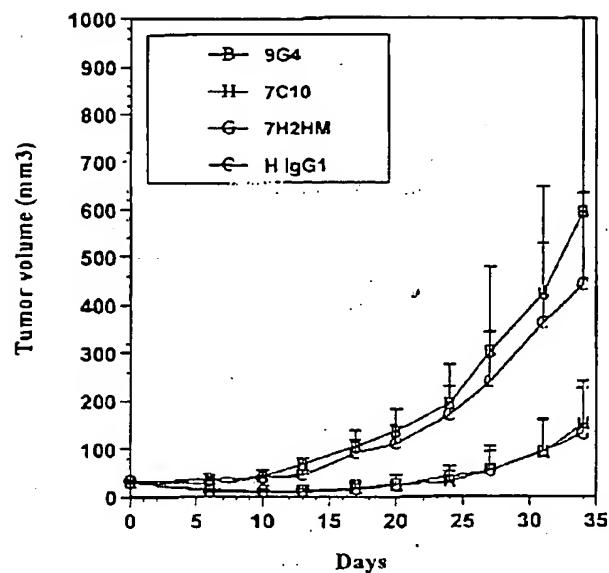


FIGURE 34A

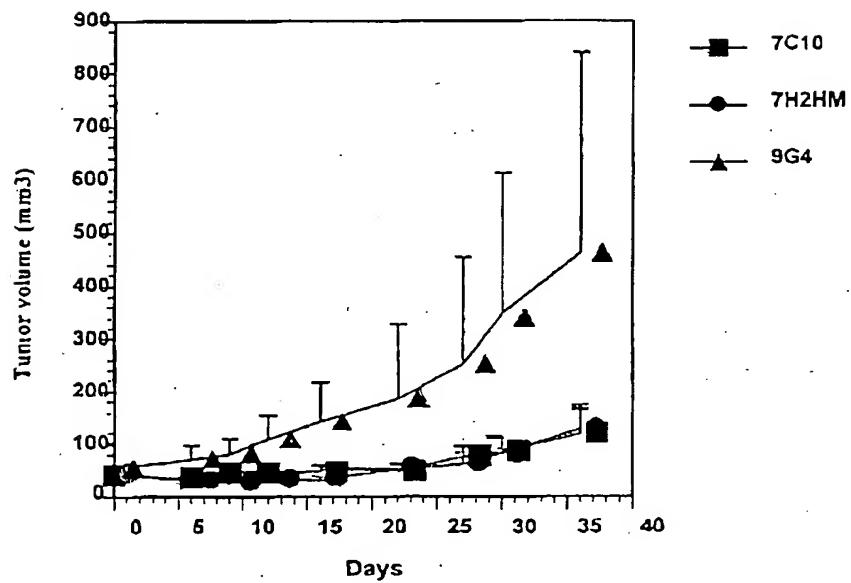


FIGURE 34B

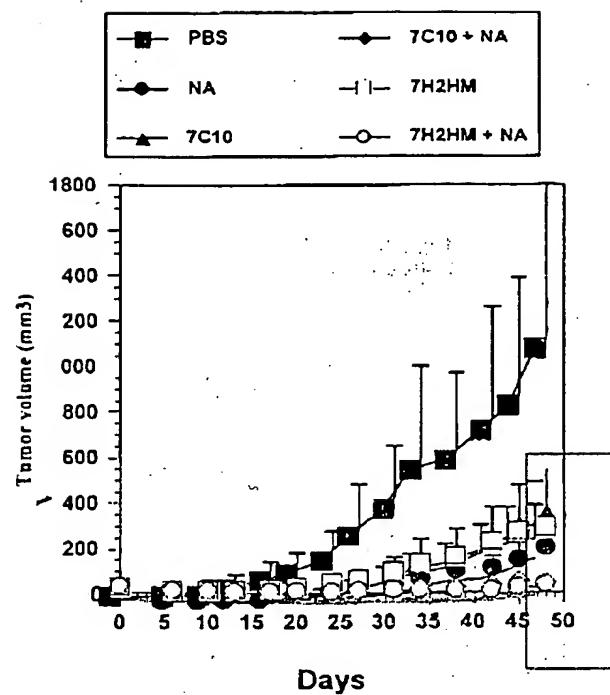


FIGURE 35A

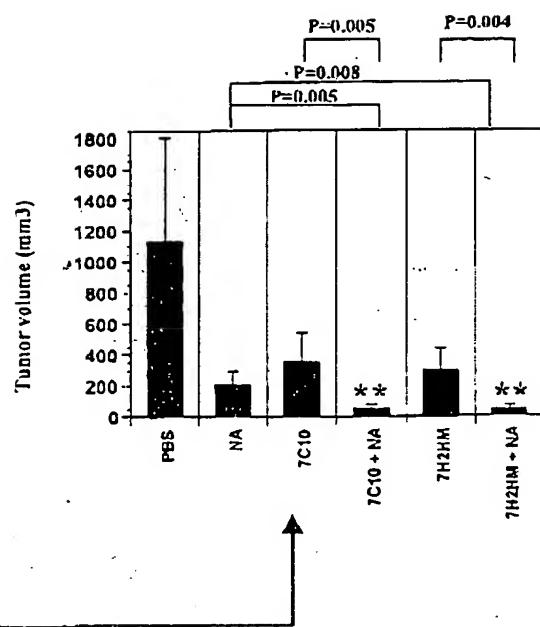


FIGURE 35B

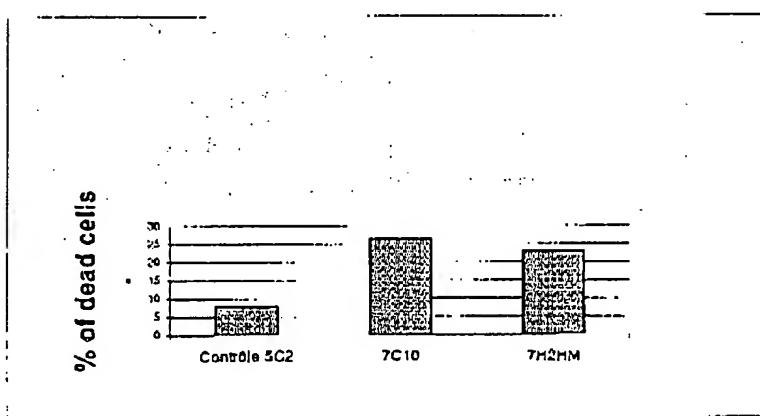


FIGURE 36

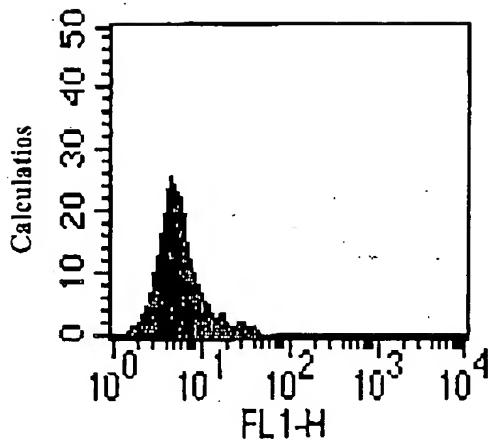


FIGURE 37A

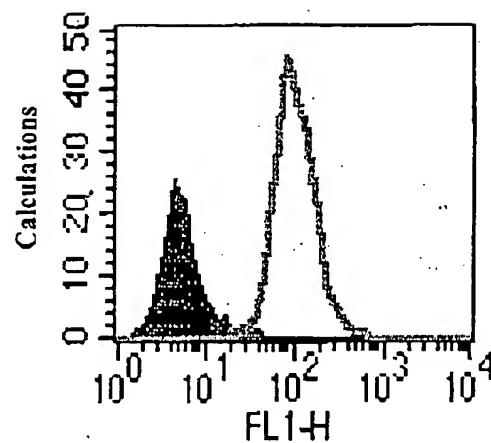


FIGURE 37B

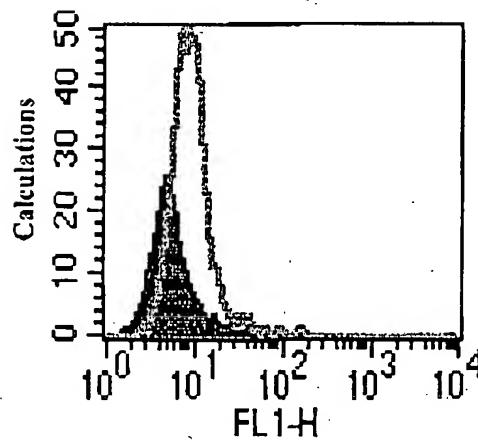


FIGURE 37C

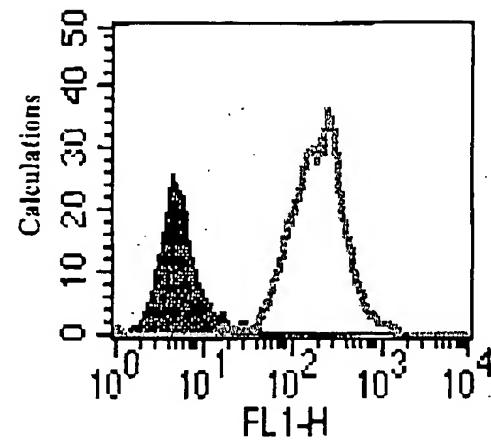


FIGURE 37D

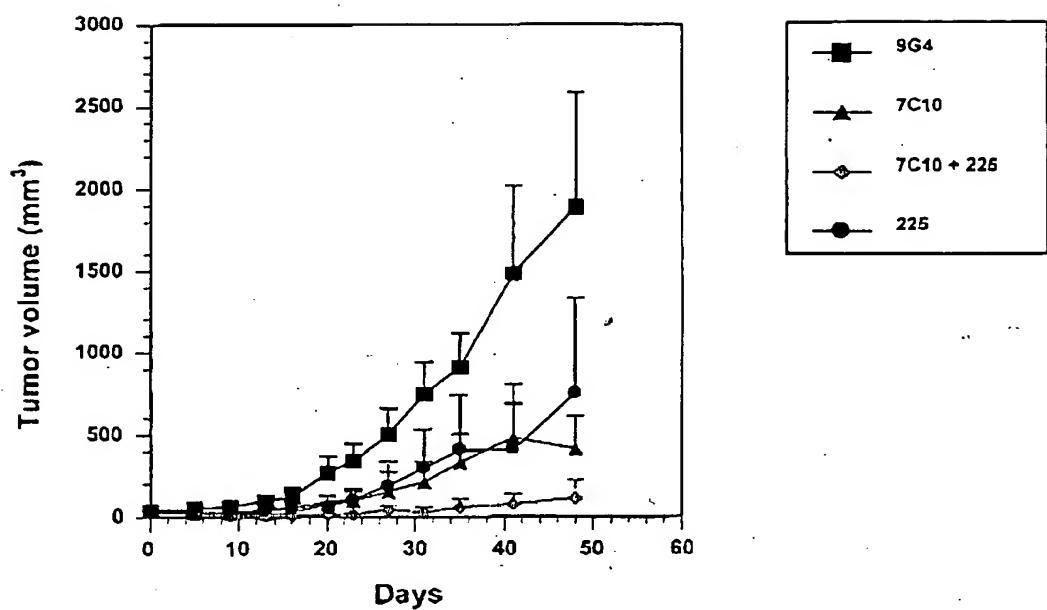


FIGURE 38

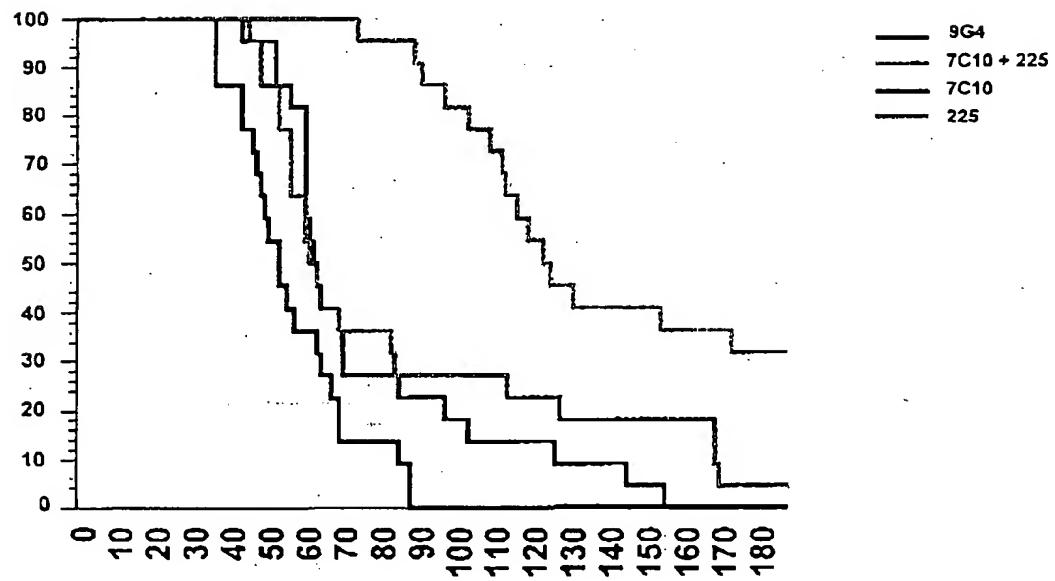


FIGURE 39

FIGURE 40A

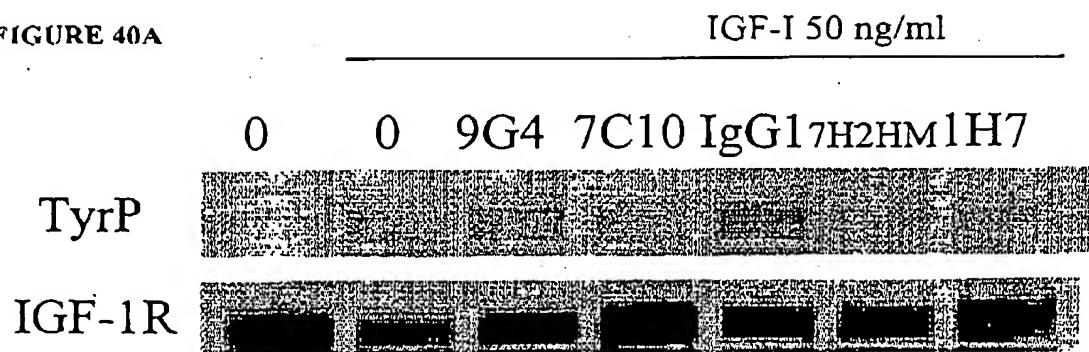


FIGURE 40B

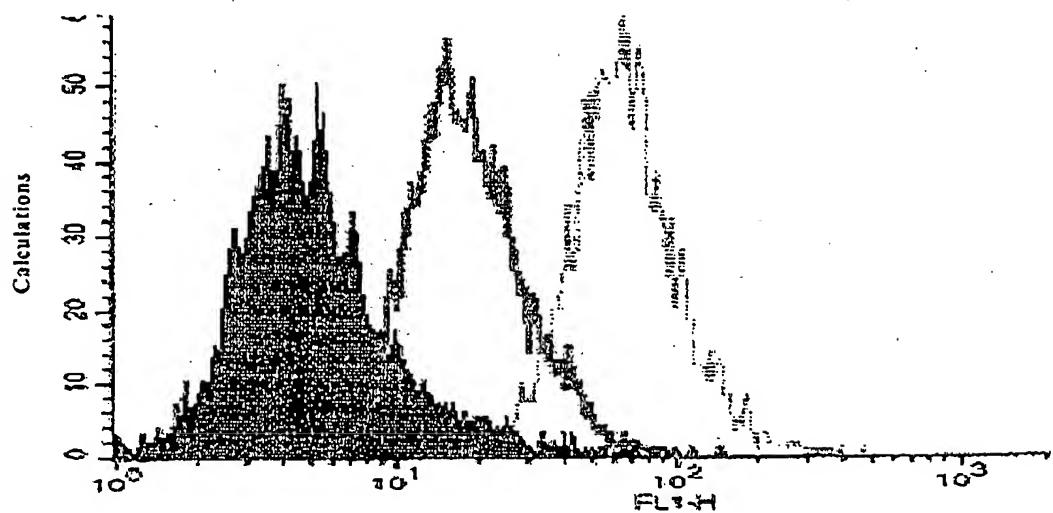
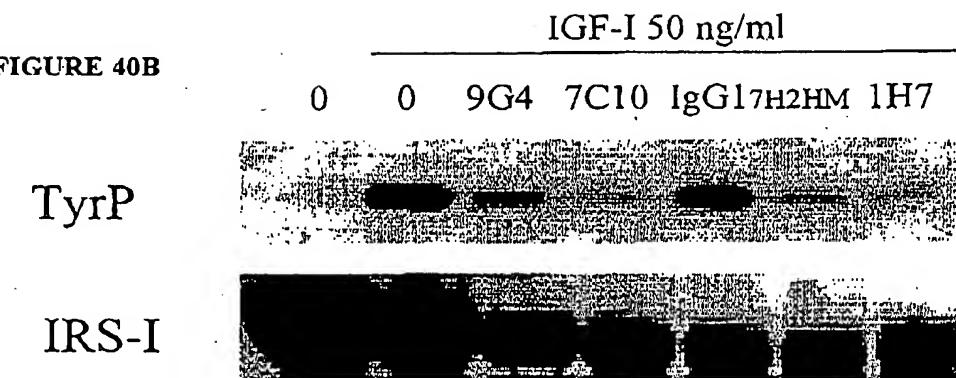


FIGURE 41

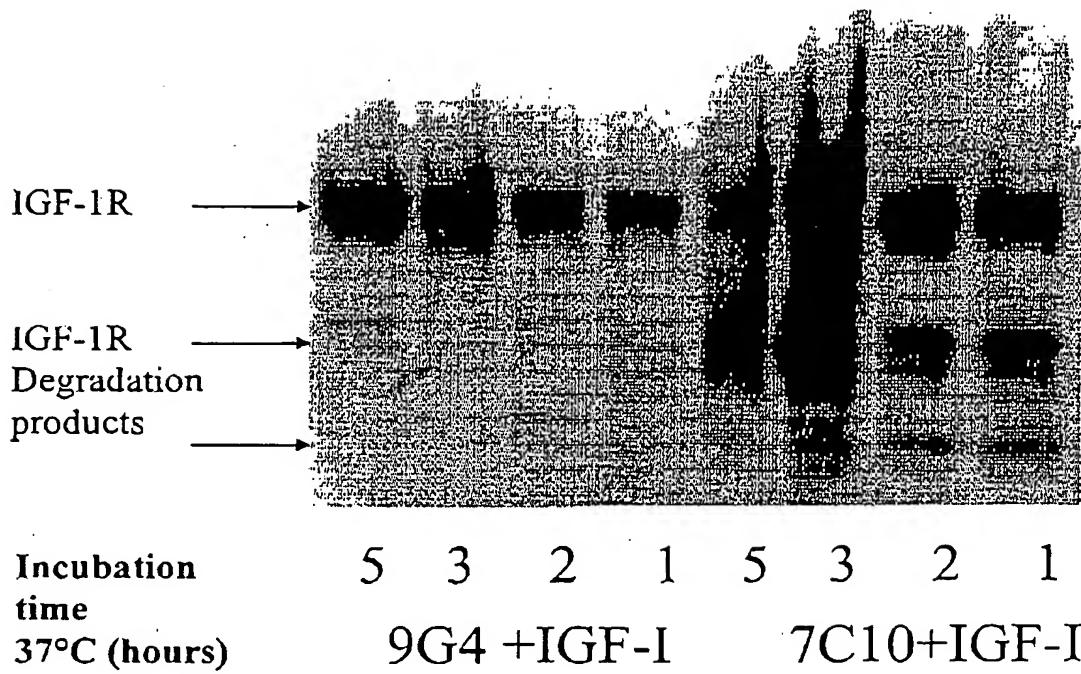


FIGURE 42A

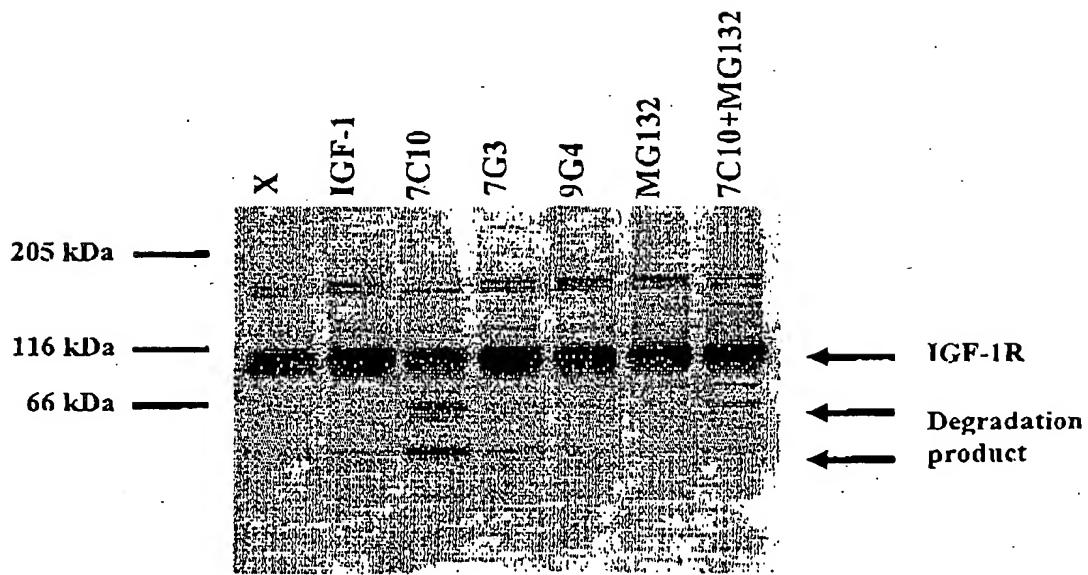


FIGURE 42B

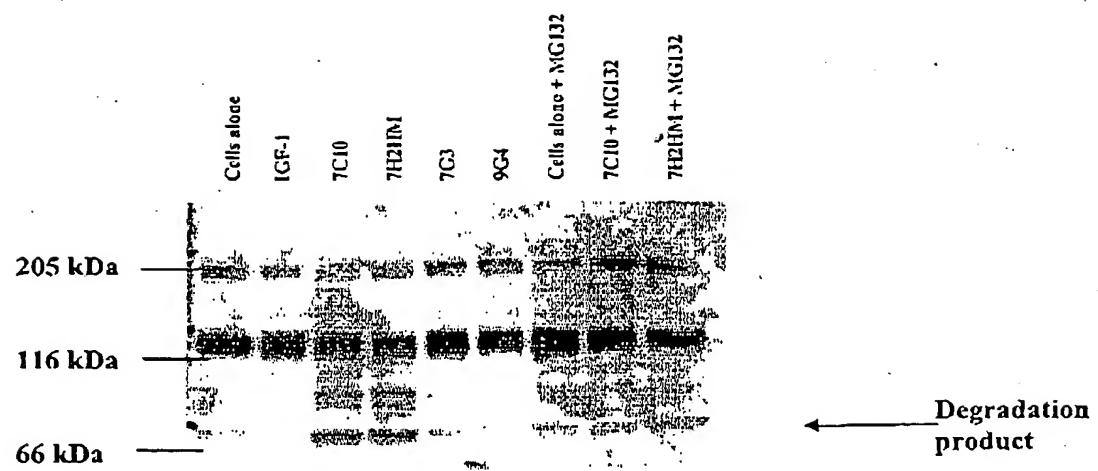


FIGURE 42C

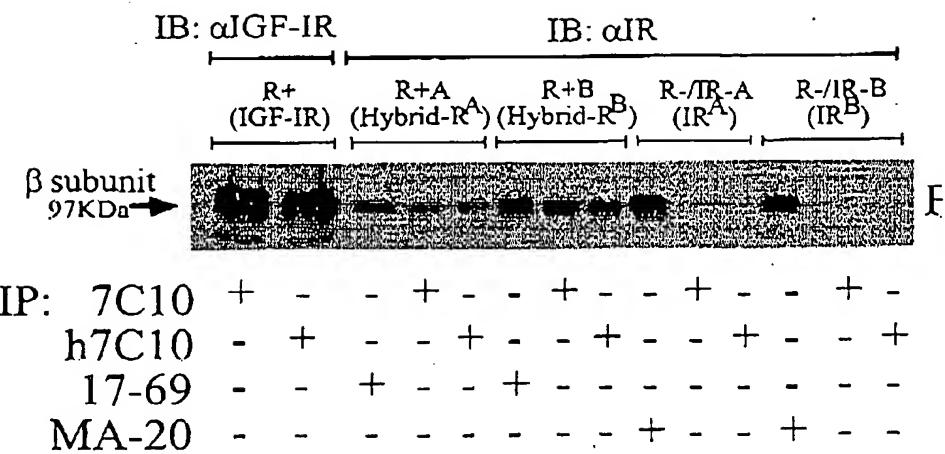


FIGURE 43A

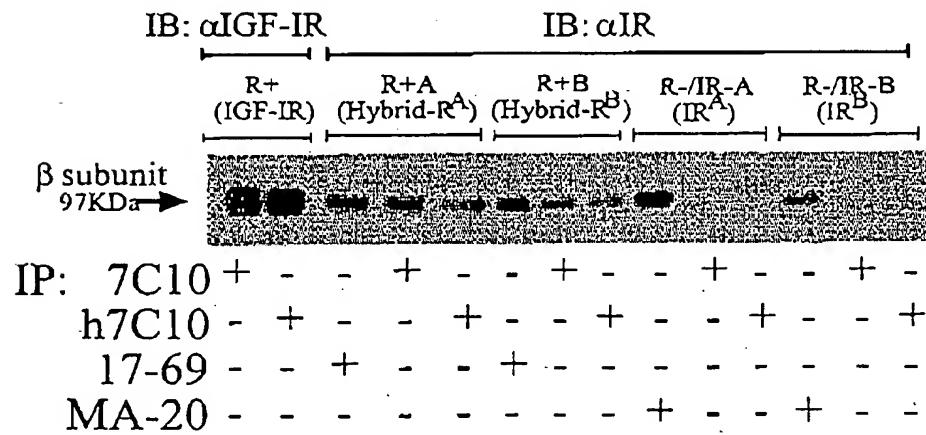


FIGURE 43B

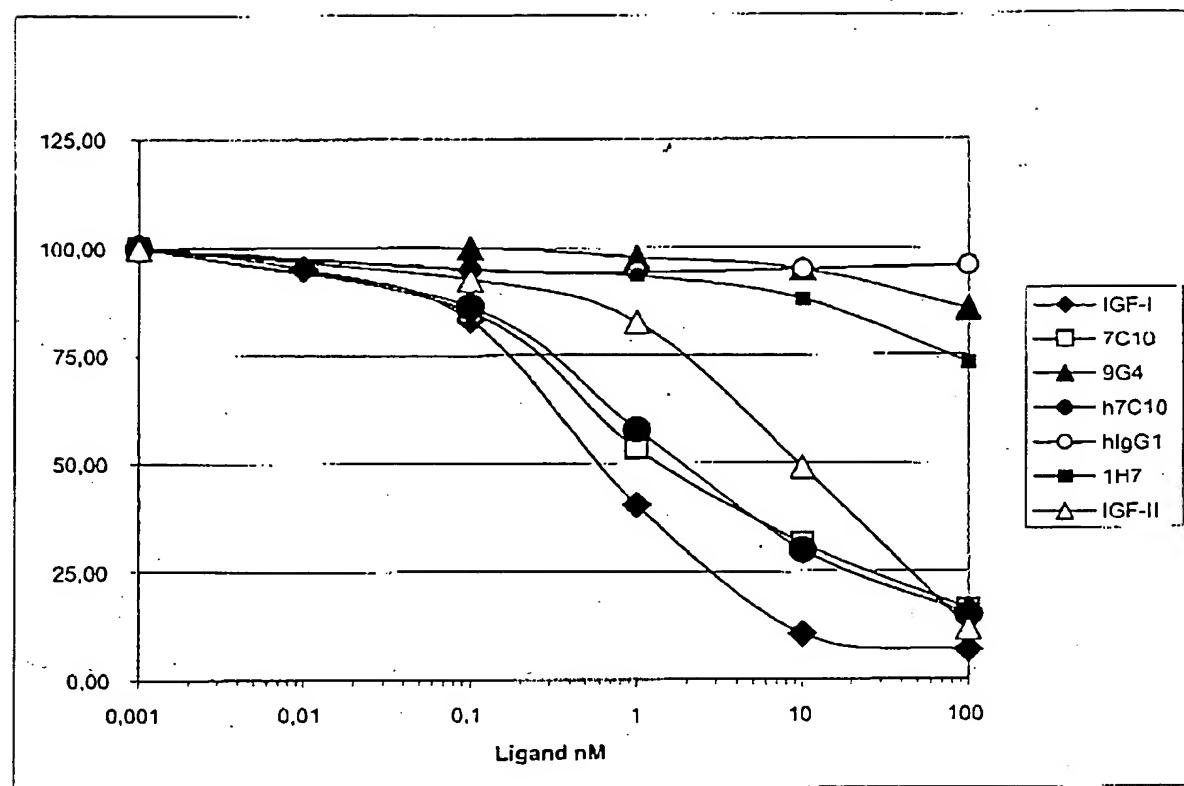


FIGURE 44

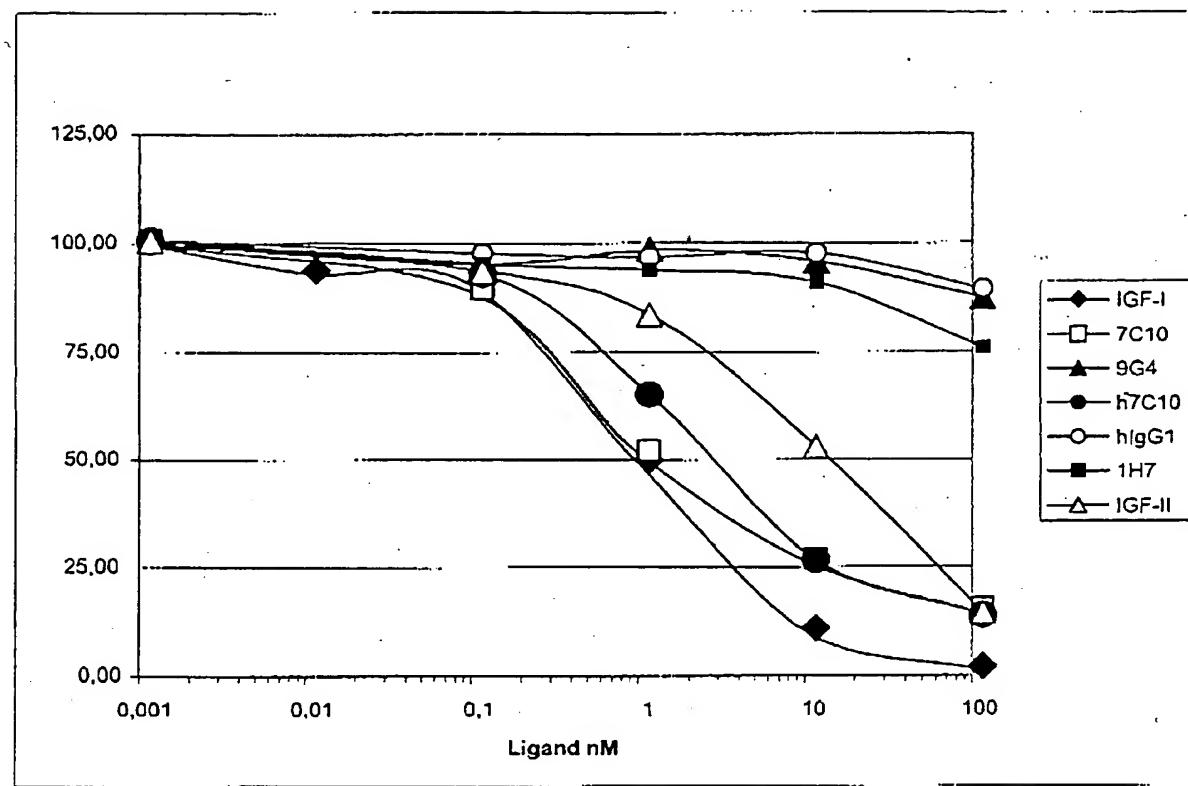


FIGURE 45

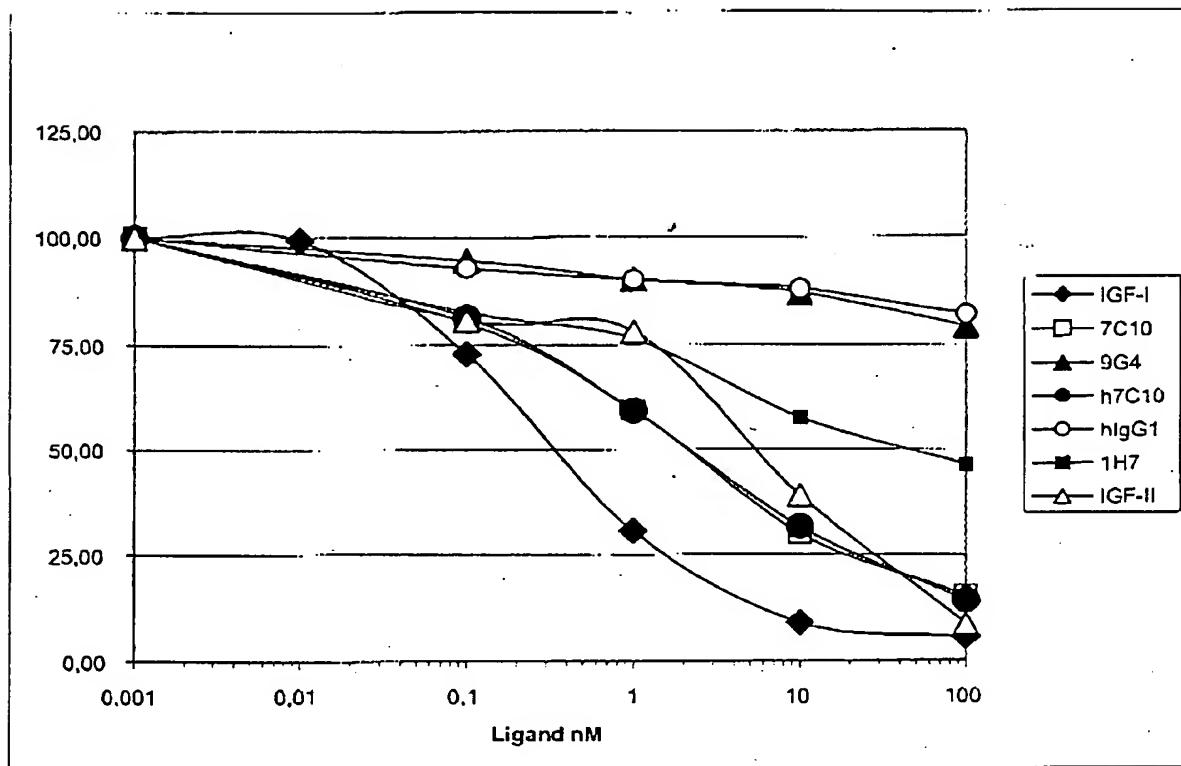


FIGURE 46

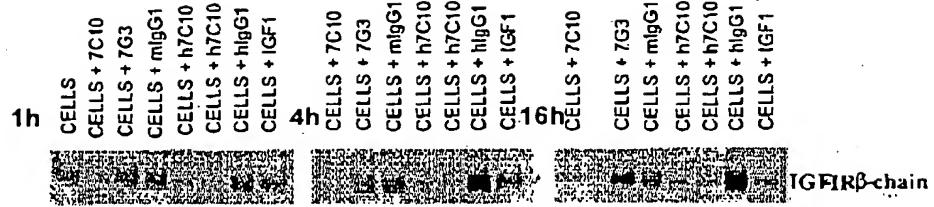


FIGURE 47A

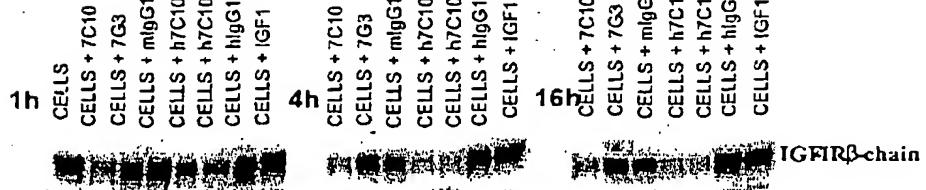


FIGURE 47B

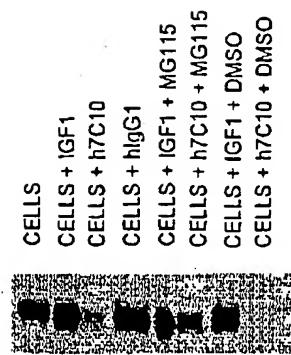


FIGURE 48

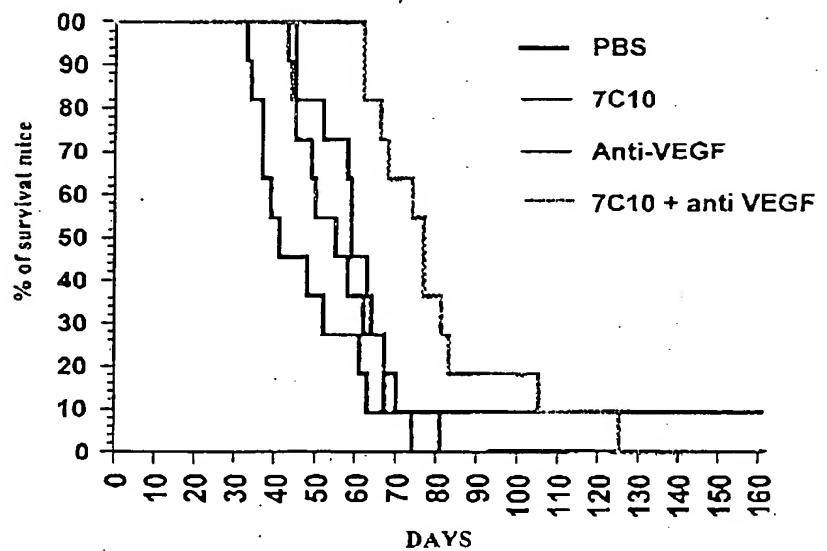


FIGURE 49

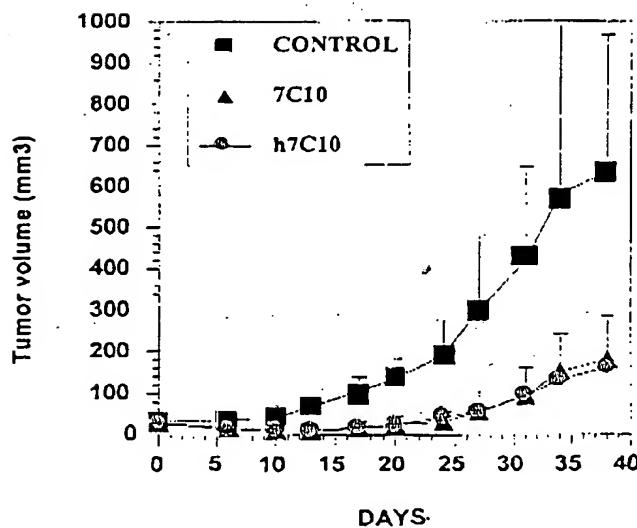


FIGURE 50

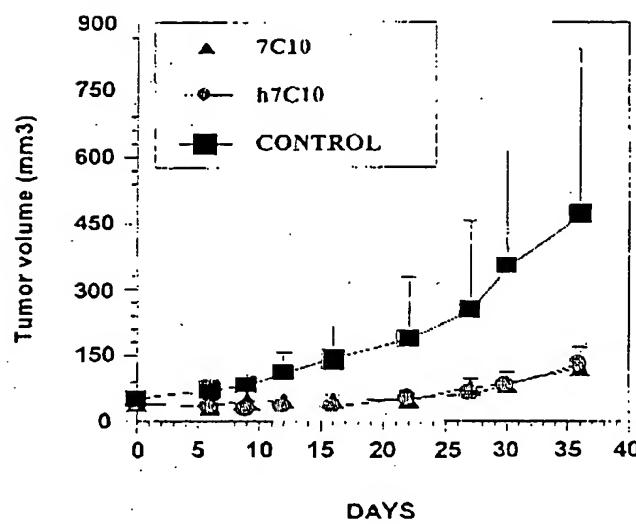


FIGURE 51

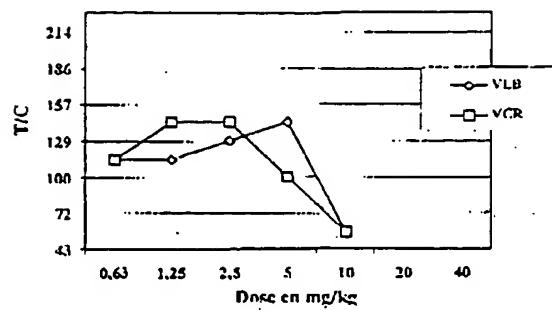


FIGURE 52

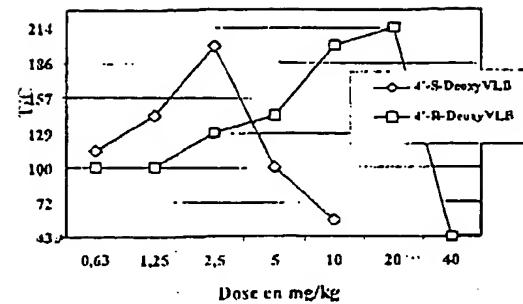


FIGURE 53

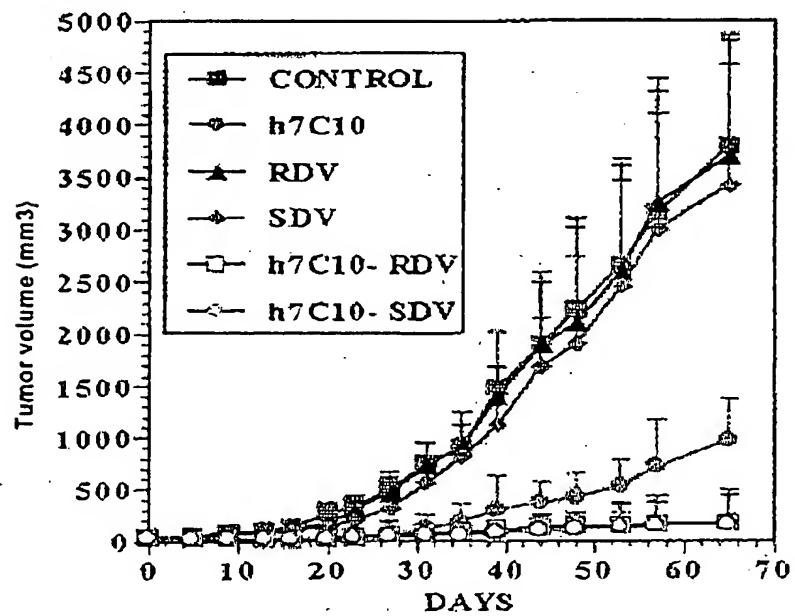


FIGURE 54